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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,414	12/13/2005	Soren Flensted Lassen	10423.204-US	9631

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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,414	LASSEN, SOREN FLENSTED	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-40* is/are pending in the application.

4a) Of the above claim(s) *33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-32 and 34-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20051213*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

Applicant's claim in the Application Data Sheet and by amendment to the first page of the specification filed 13 December 2005 to priority under 35 U.S.C. §§ 119 and 371 of the 20 June 2003 and 18 December 2003, and filing dates of the US Provisional applications, respectively, Nos. 60/531,073 and 60/549,763, as well as the 19 June 2003, 12 December 2003 and 1 March 2004 filing dates of the Danish patent applications, respectively, Nos. 2003-00911, 2003-01846, and 2004-00355, and their successor International patent application PCT/DK2004/000431 filed 2 March 2004, is hereby acknowledged.

Information Disclosure Statement

Applicant's Information Disclosure Statement [IDS] filed with the application on 13 December 2005 is hereby acknowledged.

Preliminary Amendment

Applicant's amendments to the specification and claims filed 13 December 2005 have been entered, the former providing reference to the priority documents and the latter canceling claims 1-20 and providing the new claims 21-40, which claims remain unamended in Applicant's Response to the Requirement for Restriction filed 12 December 2005.

Election

Applicant's election without traverse in the reply filed 12 December 2005 of the subject matter of Group I is acknowledged, wherein claims 21-32 and 34-40 are drawn to a genus of modified proteases having a catalytic domain the amino acid sequence of which is at least 70% identical to the amino acid sequence set forth in SEQ ID NO:43, which catalytic domain is encoded by each of SEQ ID NQS: 1, 2, 31, wherein the catalytic domain is modified by a carboxyl-terminal extension of from one to at least eight of the 15 non-polar, or uncharged amino acids glycine, alanine, valine, leucine, isoleucine, methionine, proline, phenylalanine, tryptophan, serine, threonine, asparagine, glutamine, tyrosine, and cysteine.

Because the amino acid sequence search results present in the informatic file of the instant application, accessible in the USPTO's SCORE database, demonstrate that the amino acid sequences of the protease catalytic domains of SEQ IDs NOs:37 and 41 – the "mature part of the polypeptide" referred to clauses (a) through (c) of claims 21 and 38-40 – are, respectively, 98% and 99% identical to the protease catalytic domain of SEQ ID NO:43, the requirement for restriction as between Groups 1, 4, and 5 stated in the communication mailed 8 November 2007

is hereby RESCINDED. Claims 21-32 and 34-40 are therefore examined herein to the extent that they describe polypeptides comprising proteases wherein the amino acid sequences of catalytic domains having the degrees of identity currently recited in claims 21 and 38-40 are fused to peptides providing at least three non-polar or uncharged polar amino acids within the last four amino acids of the C-terminus of the polypeptide.

Objections to the Specification

The disclosure is objected to because it contains embedded hyperlinks and/or other forms of browser-executable code at pages 1 and 5. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s). In particular, an octapeptide [QSHVQSAP] and a tetrapeptide [QSAP] are stated at page 12, lines 14 and 15, but are not identified by sequence identification numbers, even though their sequence identifiers are available in the sequence listing. Applicant's attention is directed to 37 CFR 1.821, which states:

> (d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Thus, each time that reference is made to an amino acid sequence having 4 or more amino acids, or a nucleotide sequence having ten or more nucleotides, in the specification or in the claims, it should be accompanied by the sequence identifier "SEQ ID NO:1" (see for example see Figure description starting at page 19, and page 21, last paragraph). Also at page 27, lines 1 and 2, there are two amino acid sequences, which are not accompanied by a sequence identification number.

Objections to the Claims

Claim 31 is objected to because of the following informality: The claim erroneously commences with the recitation "Claims". Appropriate correction is required.

Double Patenting: Non-Statutory

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined

application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21-32, 34, and 38-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-35 and 38-41 of the copending Application No. 10/560,224. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending application permit both the addition of the C-terminal dipeptides, tetrapeptide, and octapeptide permitted of claims 21-25 herein and the addition of a heterologous pro-region to the same proteases having the amino acid sequences recited in clause (a) of claim 21 herein. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-32 and 34-39 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

It is agreed that the specification discloses amino acid sequences of two mature proteases that share a high degree of identity with the 188-amino acid sequence of the mature protease of SEQ ID NO:43, i.e., the mature proteases of SEQ IDs NOs:41 and 37 that are, respectively, 99% identical and 98% identical over the region of 188 amino acids. The specification fails, however, to exemplify or describe the discovery or preparation of the genus of generic, mature, proteases that diverge from the disclosed 188-amino acid sequence of SEQ ID NO:34 at as

many as 30%, i.e., at as many as 56, or at as many as 80%, i.e., at as many as 36, or even as many as 90%, i.e., at even 19 positions, within the amino acid positions of SEQ ID NO:43, polynucleotides encoding such generic proteases, vectors and host cells that comprise such polynucleotides, recombinant methods of making such generic proteases utilizing such vectors and host cells, and compositions comprising such generic proteases of claims 21-32 and 34-39. Indeed, the specification fails to describe any set of 19, 36, or 56 amino acid positions within SEQ ID NO:43 that should be altered, and the alterations that might be made, to provide a sufficient number of particular, representative, species of proteases that could demonstrate possession of the claimed genera recited by claims 21, 38, and 39. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The "test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the Inventor had possession at that time of the . . . claimed subject matter", *In re Kaslow*, 217 USPQ 1089, 1096 (Fed. Cir. 1983), and, in 2001, the USPTO issued Guidelines governing its analysis of compliance with the written description requirement. In these Guidelines, the USPTO states that an applicant may comply with the written description requirement by "show[ing] that an Invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . , i.e., complete or partial structure, other physical and/or chemical properties, function characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Guidelines, 66 Fed. Reg. 1099 at 1106 (5 January 2001). The Federal Circuit adopted the USPTO's standard for determining compliance with the written description requirement In *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). The specification does not disclose the design of the very broad genera of proteases, and corresponding protease-encoding polynucleotides, embraced by claims 21-32 and 34-39 and does not otherwise disclose or suggest the nature or source of any of the generic protease s that meet the limitations of the claims.

Claims 21-32 and 34-39 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the preparation of protease catalytic domains that share at least 95% sequence identity with the amino acid sequence of the mature protease of SEQ ID NO:43, set forth from position 166 through position 353 of SEQ ID NO: 43, does not reasonably provide enablement for the preparation of protease catalytic domains that diverge as much as 70% from the amino acid sequence of the mature protease of SEQ ID NO:43, set forth from position 166 through position 353 of SEQ ID NO: 43. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use]the invention commensurate in scope with these claims.

As noted above, claims 21, 38, and 39 contemplate arbitrary assignments of any or all of amino acid substitutions, additions or deletions in a claimed, generic, protease at as many as, respectively 56, 36, and 19, amino acid positions in the 188-amino acid sequence of the mature protease of SEQ ID NO:43, i.e., from position 166 through position 353 therein. This rejection is stated under the first paragraph of the statute because the specification cannot support the introduction of such numbers of amino acid alterations in the amino acid sequence of SEQ ID NO:43 where amino acid insertions, deletions, or substitutions might occur anywhere, in any combination or in any pattern, in the mature protease amino acid sequence within SEQ ID NO:43. Indeed, neither the prior art of record herein nor Applicant's specification can identify, taken together, as many as 19 amino acid positions in the 188-amino acid sequence of the mature protease of SEQ ID NO:34 that might be altered, nor teach the nature of the alterations that might be made, that will permit resulting products to retain the function required by claim 21's preamble: "protease activity". Mere sequence perturbation cannot enable the design and preparation of a myriad of divergent proteins and provide the public with proteases that retain the activity of the mature protease of SEQ ID NO:43.

It is well settled that 35 U.S.C. § 112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (discussing factors relevant to analysis of enablement). Applying the factors discussed in *Wands* to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the amino acid sequence of the mature protease region of SEQ ID NO:34 to the extent permitted by claims 21, 38, and 39,

b) the specification lacks working examples wherein the mature protease region of SEQ ID NO:34 is altered to the extent recited permitted by claims 21, 38, and 39,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no members of the class of enzymes represented by SEQ ID NO:43 have had as many as 19 amino acids specifically identified for concurrent modification, as permitted by claim 39.

Thus the scope of subject matter embraced by the phrases, "at least 70% identical to", "at least 80% identical to", and "at least 90% identical to" is unsupported by the present specification even if taken in combination with teachings available in the prior art.

Conclusion

It is noted that amending the claims rejected above by adopting the limitation of claim 40, not subject to rejections above under 35 U.S.C. § 112, first paragraph, would overcome these rejections. In addition to provision of a Terminal Disclaimer, the claims might then be placed in condition for allowance by amending claim 31 to distinguish elected from non-elected subject matter, i.e., inserting the term "isolated" before "host cell". The claimed subject matter is free of the prior art made of record herewith because the closest prior art - the US Patents Nos. 7,179,630 and 7,208,310 and the several corresponding published International applications cited in the accompanying PTO-Form 892 - is commonly-assigned and shares common priority dates for disclosures of the encoding nucleic acid sequence, 19 June 2003, and encoded amino acid sequence, 12 December 2003, of the elected and examined mature *Nocardiopsis* sp. protease of SEQ ID NO:43. The *Nocardiopsis* sp. protease amino acid sequence of Mitsuiki et al., also made of record with the accompanying PTO-Form 892 has an electronic publication date after the earliest, 19 June 2003, priority date herein for the inherent disclosure of the mature *Nocardiopsis* sp. protease of SEQ ID NO:43 herein. The International publication WO 01/58276, made of record with Applicant's Information Disclosure Statement discloses a protease having an amino acid sequence only 55% identical to the elected protease having the amino acid sequence set forth in SEQ ID NO:43 herein.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr Bragdon, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

/Nashed/
Nashaat T. Nashed, Ph.D.
Primary Examiner, Art Unit 1656

William W. Moore
7 January 2008